D 4 cont'd

each b is an integer from 1 to 5; and

c is an integer value from 2 to 10.

REMARKS

Claims 1- 48 are pending in the instant application. By this communication, Applicants cancel claims 6-37 and 39-41, amend claims 1-4, 38, and 42-48, and add new claim 49. The new and amended claims are commensurate in scope with the claims as filed, and do not introduce new matter or require a new search. For example, the definition of R1 in claim 1 is equivalent to that present in originally filed claim 41, while new claim 49 represents the subject matter previously reflected in claim 41, and is introduced to assist the examiner in understanding the claimed invention.

Notwithstanding the foregoing, Applicants expressly reserve the right to prosecute subject matter no longer or not yet claimed in one or more applications that may claim priority hereto. Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the following comments.

Non-Art Related Remarks

Restriction/Election

In Paper No. 17, the Examiner indicated that only the claims of Group I, as described in Paper No. 3, are under consideration. Applicants respectfully submit that the Examiner has misidentified the claims in Group I as being claims 1-4 and 41-48. The correct grouping includes claims 1-5, 38, and 41-48. Applicants, therefore, respectfully request clarification of the claims under consideration.

Drawings:

Applicants respectfully submit corrected formal drawings herewith.

Claim Informalities

Applicants gratefully acknowledge the claim informalities to which the Examiner has drawn Applicants' attention, and respectfully submit that the foregoing amendments to the claims clarify these informalities. Each is addressed separately below.

The Examiner indicated that elected species "ImImHpPy-γ-ImPyPyPy-β-Dp" was allegedly not included within the scope of claim 1, because -β-Dp was not included in the definition of the polyamide. Applicants respectfully submit that, because -β-Dp is within the definition of R_1 in claim 1 as amended herein, the objection is rendered moot.

The Examiner also indicated that claims 41-48, which depend from claim 1, were drawn to polyamide compositions, and not the methods of claim 1. By the present communication, claim 41 is cancelled, claims 42-45 amended to method claims, and claims 46-48 to refer to compositions using product-by-process language. Applicants respectfully submit that the foregoing amendments render the objection moot.

The Examiner also requested clarification of the abbreviations "Im," "Hp," "Py," "β," "A," "G," "C," and "T"; and the phrase "specificity greater than or equal to ten" used in the claims. Applicants respectfully submit that the foregoing amendments render the objection moot. These amendments are not further limiting on the claims, but instead simply provide the appropriate definition from the specification for each of these terms and phrases. Applicants respectfully submit that these amendments render the objection moot.

The Examiner noted that the parameter "n" is used in claim 41 (now claim 49) without further definition. Applicants respectfully submit that new claim 49 renders the objection moot. Support for a definition of "n" as being an integer from 1 to 2 can be found, *e.g.*, in the use of β-alanine and γ-aminobutyric acid in Tables 20-179.

Finally, the Examiner requested that periods within claim 1 be replaced with parentheses, and misspellings in claims 1 and 47 be corrected. Applicants respectfully submit that the foregoing amendments render the objection moot.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable consideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date December 4, 2001

By _____

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Appendix A: Marked-up claims, indicating the amendments. Clams that have not been amended are provided herewith, marked as "Reiterated."

1. (Amended) A method for designing a specific polyamide

$$X_1X_2 \ldots X_m\text{-}\gamma\text{-}X_{(m+1)} \ldots X_{(2m-1)}X_{2m}\text{-}R_1$$

wherein

X_1, X_2, X_m, $X_{(m+1)}$, $X_{(2m-1)}$, and X_{2m} are carboxamide residues forming carboxamide binding pairs X_1/X_{2m}, $X_2/X_{(2M-1}$, $X_M/X_{M+1)}$,

[and] γ is [γ-aminobuytic] γ-aminobutyric acid or 2,4 diaminobutyric acid, and [Dp]

R_1 is $-NH(CH_2)_{0\text{-}100}NR_2R_3$, $-NH(CH_2)_{0\text{-}100}CO\ NH(CH_2)_{0\text{-}100}NR_2R_3$, or $-NHR_2$, where R_2 and R_3 are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl, $C_{1\text{-}100}$ alkyl, $C_{1\text{-}100}$ alkylamine, $C_{1\text{-}100}$ alkyldiamine, $C_{1\text{-}100}$ alkylcarboxylate, $C_{1\text{-}100}$ alkenyl, a $C_{1\text{-}100}$ alkynyl, and $C_{1\text{-}100}$ alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins, polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports, oligodeoxynucleotides, N-ethylnitrosourea, fluorescein, bromoacetamide, iodoacetamide, DL-α-lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthrinilic acid, avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-(psoraen-8-yloxy)-butyrate, taartaric acid, and (+)-α-tocopheral [dimethylaminopropylamide], suitable for use as a DNA-binding ligand that is selective for identified target DNA-sequences 5'-$WN_1N_2 \ldots N_mW$-3' where m is an integer having a value from 3 to 6, the method comprising [the steps of]:

(a[.]) identifying a target sequence of double stranded DNA having the form 5'-WN_1N_2 . . . N_mW-3', N_1N_2 . . . N_m being the sequence to be bound by carboxamide residues, wherein each N is independently chosen from the group A, G, C, and T, each W is independently chosen from the group A and T, and m is an integer having a value from 3 to 6;

(b[.]) representing the identified sequence as 5'-W*ab* ... *x*W-3', wherein *a* is a first nucleotide to be bound by the X_1 carboxamide residue, *b* is a second nucleotide to be bound by the X_2 carboxamide residue, and *x* is the corresponding nucleotide to be bound by the X_m carboxamide residue;

(c[.]) defining *a* as A, G, C, or T to correspond to the first nucleotide to be bound by a carboxamide residue in the identified sequence;

(d[.]) selecting Im as the X_1 carboxamide residue and Py as the X_{2m} carboxamide residue if a = G;

(e[.]) selecting Py as the X_1 carboxamide residue and Im as the X_{2m} carboxamide residue if *a* = C;

(f[.]) selecting Hp as the X_1 carboxamide residue and Py as the X_{2m} carboxamide residue if *a* = T;

(g[.]) selecting Py as the X_1 carboxamide residue and Hp as the X_{2m} carboxamide residue if *a* = A; and

(h[.]) repeating steps c – g for *b* through *x* until all carboxamide residues are selected;

wherein Im is N-methylimidazole, Hp is , Py is N-methylpyrrole, A is adenine, G is guanine, C is cytosine, and T is thymine.

2. (Amended) The method of claim 1 further comprising the step of synthesizing the polyamide

$$[X_1X_2 \ldots X_m\text{-}\gamma\text{-}X_{(m-1)} \ldots X_{(2m-1)}X_{2m}].$$

3. (Amended) The method of claim 2 further comprising the step of determining if the binding affinity of the polyamide to the identified target sequence is subnanomolar.

4. (Amended) The method of claim 1 further comprising the step of determining if the [sequence specificity of the] polyamide [is] exhibits a binding affinity that is at least [greater or equal to] ten-fold higher for said identified target sequence compared to a non-target DNA sequence.

5. (Reiterated) The method of claim 2 further comprising the step of replacing at least one pyrrole residue with a β-alanine residue.

38. (Amended) A polyamide composition produced by the method of claim 2 wherein one carboxamide binding pair is β/β, wherein β is β-alanine.

41. (Cancelled)

42. (Amended) The [polyamide] method of claim 1 wherein the [duplex] identified target DNA sequence is a regulatory sequence.

43. (Amended) The [polyamide] method of claim 1 wherein the [duplex] identified target DNA sequence is a promoter sequence.

44. (Amended) The [polyamide] method of claim 1 wherein the [duplex] identified target DNA sequence is a coding sequence.

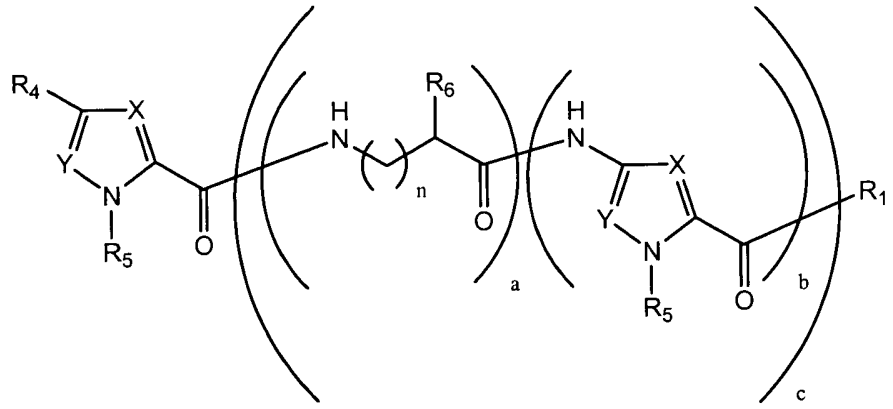
45. (Amended) The [polyamide] method of claim 1 wherein the [duplex] identified target DNA sequence is a non-coding sequence.

46. (Amended) [The] A polyamide composition produced by the method of claim [1] 2 wherein the binding of the carboxamide binding pairs to the identified target DNA sequence modulates the expression of a gene.

47. (Amended) A composition [conprising] comprising an effective amount of [the] a polyamide produced by the method of claim [1] 2 and a pharmologically suitable excipient.

48. (Amended) A diagnostic kit comprising [the] a polyamide produced by the method of claim [1] 2.

49. (New) A polyamide designed by the method of claim 1, having the structure:



wherein

R_4 is selected from the group consisting of H, NH_2, SH, Cl, Br, F, N-acetyl, and N-formyl;

each R_5 is independently selected from the group consisting of H, $(CH_2)_{0-6}CH_3$, $(CH_2)_{0-6}NH_2$, $(CH_2)_{0-6}SH$, $(CH_2)_{0-6}OH$, $(CH_2)_{0-6}N(R_7)_2$, $(CH_2)_{0-6}OR_7$, and $(CH_2)_{0-6}SR_7$, wherein R_7 is $(CH_2)_{0-6}CH_3$, $(CH_2)_{0-6}NH_2$, $(CH_2)_{0-6}SH$, or $(CH_2)_{0-6}OH$;

each R_6 is independently selected from the group consisting of H, NH_2, OH, SH, Br, Cl, F, OMe, CH_2OH, CH_2SH, and CH_2NH_2;

R_1 is $-NH(CH_2)_{0-100}NR_2R_3$, $-NH(CH_2)_{0-100}CO\ NH(CH_2)_{0-100}NR_2R_3$, or $-NHR_2$, where R_2 and R_3 are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl, C_{1-100} alkyl, C_{1-100} alkylamine, C_{1-100} alkyldiamine, C_{1-100} alkylcarboxylate, C_{1-100} alkenyl, a C_{1-100} alkynyl, and C_{1-100} alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins, polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports, oligodeoxynucleotides, N-ethylnitrosourea, fluorescein, bromoacetamide, iodoacetamide, DL-α-lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthrinilic acid, avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-(psoraen-8-yloxy)-butyrate, taartaric acid, and (+)-α-tocopheral;

each X and Y are independently selected from the group consisting of N, CH, COH, CCH_3, CNH_2, CCl, and CF;

each n is an integer from 1 to 2;

each a is an integer from 0 or 1;

each b is an integer from 1 to 5; and

c is an integer value from 2 to 10.